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KLAUBER & JACKSON 411 HACKENSACK AVENUE HACKENSACK, NJ 07601			EXAMINER WEHBE, ANNE MARIE SABRINA	
			ART UNIT	PAPER NUMBER
			1632	
DATE MAILED: 01/14/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/982,120

Applicant(s)

SIMON ET AL.

Examiner

Anne Marie S. Wehbe

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-53 is/are pending in the application.
- 4a) Of the above claim(s) 33-51 and 53 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-32 and 52 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 October 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *Notice to Comply*.

### **DETAILED ACTION**

Applicant's response to the restriction requirement received on 10/10/03 has been entered. Applicant's election with traverse of the subject matter of Group I, claim 1-16, and 52 is noted. Claims 1-53 are pending in the instant application. Of these, claims 33-51 and 53 have been withdrawn from consideration as being directed to subject matter non-elected with traverse in applicant's submission dated 10/10/03. Claims 1-32, and 52 are currently under examination. An action on the merits follows.

### **Restriction/Election**

The applicant has traversed the restriction requirement arguing that a search of group I would require a search of the identical classes as Group II and that the examination of Group I and II together would not present a serious burden to the examiner. In view of applicant's arguments, the subject matter of Groups I and II are hereby rejoined. Thus, as noted above, claims 1-32, and 52 are currently under examination as the elected subject matter. Regarding the restriction requirement between Groups I and II and Groups III-V, the applicant has not made any specific arguments regarding the grounds for restriction between these inventions, thus the restriction requirement between Groups I and II and Groups III-V is maintained. Therefore, the requirement is still deemed proper and is made FINAL.

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**Nucleotide and/or Amino Acid Sequences**

This application discloses an amino acid sequence on page 14, line 14. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures which is attached to this communication. In particular, the sequence listed on page 14 is not identified by SEQ ID NO.

Full compliance with the sequence rules is required in response to this Office Action. A complete response to this office action should include both compliance with the sequence rules, which included amendment of the specification on page 14 to include a SEQ ID NO., and a response to the rejections set forth below. Failure to comply with **both** these requirements in the time period set forth in this office action will be held non-responsive. Applicant is requested to return a copy of the attached Notice To Comply with the response.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-16 and 52 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims as written recite genetically-modified

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mammals. As such, the claims read on genetically modified humans. Human beings are not patentable subject matter. This rejection can be overcome by amending the claims to recite "non-human" mammals.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 10, 11, 15-17, 26-27, and 31-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification discloses a chimeric immunoglobulin gene comprising an immunoglobulin component and at least one detectable protein or peptide which is a protein or polypeptide that is capable of quenching fluorescence or which is a combination of autofluorescent, enzymatically active, or visibly detectable proteins or peptides. Please note that the rejection of claims 11, 15-16, 27, and 31-32 under 35 U.S.C. 112, second paragraph, below discusses the fact that the claims are indefinite and confusing in that it is unclear whether the applicant intends to recite that the chimeric immunoglobulin gene comprises nucleic acid sequence for two separate detectable markers or whether the marker itself is in fact a fusion between two different detectable marker genes. The specification does not disclose or provide any written description for proteins or polypeptides

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capable of quenching fluorescence, or provide any description of detectable proteins that are a fusion between two different detectable markers, or specifically green fluorescent protein and alkaline phosphatase. The specification further fails to disclose the nucleic acid sequences which encode these proteins for using in making the claimed genetically modified cells and mammals. The specification discloses several detectable marker genes which encode autofluorescent or enzymatically active proteins or polypeptides, the specification fails to provide sufficient description of the physical or chemical properties of any protein that quenches fluorescence such that protein molecules or nucleic acid molecules encoding these proteins which meet these requirements could be identified. The specification also fails to provide any guidance as to making chimeric detectable markers that are the result of a fusion of two different detectable marker genes, or provide any guidance as to the physical or biological properties of any such combined molecules. Based on the breadth of the claims as written, the specification lacks written description for the identity of fluorescence quenching proteins and chimeric detectable proteins.

*Vas-Cath Inc. V. Mahurkar*, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of ‘written description’ inquiry, whatever is claimed” (see page 1117). In addition, the Revised Interim Guidelines state “ when there is substantial variation with the genus, one must describe a sufficient variety of species to reflect the variation within the genus .....In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus” (Column 2, page 71436, or the Revised Interim Guidelines for Written

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Description). Case law concurs, stating, "simply describing large genus of compounds is not sufficient to satisfy written description requirement as to particular species or sub-genus" *Fujikawa v. Wattanasin*, 39 USPQ2d 1895 (CA FC 1996). By failing to identify or describe any protein or nucleic acid encoding a protein which quenches fluorescence or any chimeric detectable protein or nucleic acid comprising a fusion between two detectable proteins, the specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). Adequate written description requires more than a mere statement that an element is part of the invention. Based on the applicant's specification, the skilled artisan cannot envision the detailed chemical structure of molecules which meet the claim requirements. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. See *Fiers v. Revel*, 25 USPQ2d 1602 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Claims 1-17, 26-27, 31-32, and 52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention as claimed.

In regards to claims 1, 10, 11, 15-17, 26-27, and 31-32, the above rejection states that the subject matter of these claims is not adequately described by the disclosure of the instant specification. Since the specification does not identify or describe any protein or nucleic acid encoding a protein which quenches fluorescence or any chimeric detectable protein or nucleic

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acid comprising a fusion between two detectable proteins, the specification fails to enable how to make or use the invention as claimed in regards to these embodiments.

The specification does not provide an enabling disclosure for producing any and all genetically modified mammals other than transgenic mice. The specification teaches genetically modified “knock-in” mammals which comprise a chimeric rearranged immunoglobulin heavy and/or light chain gene wherein nucleic acid encoding a detectable protein or peptide has been inserted at the C-terminus of the immunoglobulin gene through homologous recombination. The specification discloses that embryonic stem cells or other types of embryonal cells can be transfected *in vitro* with a polynucleotide vector capable of homologously recombining into the genome, injected into a blastocyst, and implanted into a pseudopregnant female animal resulting in progeny with transgenic DNA inserted into one or more copies of the targeted gene of interest. The specification does not provide guidance for identifying and isolating embryonic stem cells from species other than the mouse, or for identifying other embryonal cells which are capable of contributing to the germline of any animal. At the time of filing, Campbell et al. teaches that, “[i]n species other than the mouse the isolation of ES cells has proved more difficult. There are reports of ES-like cell lines in a number of species....However, as yet there are no reports of any cell lines which contribute to the germ line in any species other than the mouse” (Campbell et al. (1997) *Theriology*, Vol. 47 (1), page 65, paragraph 2). Thus, based on the art recognized unpredictability of isolating and using embryonic stem cells or other embryonal cells from animals other than mice to produce transgenic animals, and in view of the lack of guidance provided by the specification for identifying and isolating embryonal cells which can contribute to the germ line of any non-human mammal other than the mouse, such as dogs, cows, or



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platypus, the skilled artisan would not have reasonably predicted success in generating any and all non-human transgenic mammals using ES cell technology. Thus, it would have required undue experimentation at the time of filing for the skilled artisan to practice the scope of the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claims 1 and 17 recite genetically-modified immune cells or mammals capable of expressing a chimeric immunoglobulin gene, “..comprising at least one detectable protein or peptide fused with a gene expressing an immunoglobulin component..”. Claims 2-16, and 18-32 depend on claims 1 and 17 and are thus included in this rejection. It is unclear as to whether the applicant intends to claim that a protein or peptide is fused directly to a nucleic acid gene or whether the applicant intends to claim that the chimeric immunoglobulin gene comprises a nucleic acid sequence encoding at least one detectable protein or peptide operably linked to a gene expressing an immunoglobulin component. Thus, the metes and bounds of the claims are confusing. Amendment of the independent claims to insert , “ a polynucleotide sequence encoding ....” after the word “comprising” would overcome this rejection.

Claims 11, 15-16, 27 and 31-32 are further rejected for indefiniteness based on their recitation that , “said at least one detectable protein is a combination of an autofluorescent

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protein or peptide and an enzymatically-active protein or peptide". It is unclear from this language whether the applicant means that the combination is a single protein which is both autofluorescent and enzymatically active, such as chimeric GFP/alkaline phosphatase, or whether the applicant intends the chimeric immunoglobulin to include two separate detectable markers, one autofluorescent and one enzymatically active. If the latter is the intended meaning, please note that the claims do not reflect this alternative. The claims as written appear to read on a single detectable protein and not two proteins. Therefore, the claims as written are confusing and the metes and bounds of the claims cannot be determined.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-19, and 22-25 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,202,238 (1993), hereafter referred to as Fell et al. The applicant claims genetically-modified immune cells which comprise a chimeric immunoglobulin gene comprising a gene expressing an immunoglobulin component linked to a polynucleotide encoding a detectable protein or peptide, wherein the immunoglobulin component includes kappa or lambda light chain components, or heavy chain components. The applicant further claims said cells wherein the

polynucleotide encoding the detectable protein is present at the C-terminus of the gene product and located in exon G1.

Fell et al. teaches genetically modified antibody producing cells which have undergone homologous recombination to replace a component of the immunoglobulin genes with all or a portion of a human variable or constant gene linked to an enzyme or substrate such as betagalactosidase, alkaline phosphatase, or horseradish peroxidase (Fell et al., column 11, lines 24-66, and column 12, lines 1-12). Fell et al. discloses that the antibodies produced by these modified cells can be used as labeled antibodies in diagnostic assays without further modification (Fell et al., column 11, lines 55-66). Fell et al. further teaches that the replacement gene can be inserted into either or both of the light chain or heavy chain immunoglobulin genes (Fell et al., column 10). Fell et al. further teaches that the replacement gene is linked to the C-terminus of the chimeric immunoglobulin (Fell et al., Figures 1B + 1C). Fell et al. also provides a specific embodiment where the replacement gene encodes all or a portion of IgG1, such that a linked enzyme would therefore be present in exon G1 (Fell et al., column 14, lines 55-67). Thus, by teaching all of the limitations of the claims as written, Fell et al. anticipates the instant invention as claimed.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 20-21 and 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,202,238 (1993), hereafter referred to as Fell et al., in view of Casey et al. (June 2000) Prot. Engineer., Vol. 13(6) 445-452. The applicant claims genetically-modified immune cells which comprise a chimeric immunoglobulin gene comprising a gene expressing an immunoglobulin component linked to a polynucleotide encoding a detectable protein or peptide, wherein the immunoglobulin component includes kappa or lambda light chain components, or heavy chain components. The applicant further claims said cells wherein the polynucleotide encoding the detectable protein is present at the C-terminus of the gene product with a flexible linked therebetween and located in exon G1. In addition, the applicant claims said cells wherein the detectable marker is an autofluorescent protein such as green fluorescent protein (GFP).

Fell et al. teaches genetically modified antibody producing cells which have undergone homologous recombination to replace a component of the immunoglobulin genes with all or a portion of a human variable or constant gene linked to a enzyme or substrate such as

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betagalactosidase, alkaline phosphatase, or horseradish peroxidase (Fell et al., column 11, lines 24-66, and column 12, lines 1-12). Fell et al. discloses that the antibodies produced by these modified cells can be used as labeled antibodies in diagnostic assays without further modification (Fell et al., column 11, lines 55-66). Fell et al. further teaches that the replacement gene can be inserted into either or both of the light chain or heavy chain immunoglobulin genes (Fell et al., column 10). Fell et al. further teaches that the replacement gene is linked to the C-terminus of the chimeric immunoglobulin (Fell et al., Figures 1B + 1C). Fell et al. also provides a specific embodiment where the replacement gene encodes all or a portion of IgG1, such that a linked enzyme would therefore be present in exon G1 (Fell et al., column 14, lines 55-67).

Fell et al. differs from the instant invention by not specifically teaching that a flexible linked is present between the immunoglobulin region and the detectable protein. Casey et al. supplements Fell et al. by teaching the construction of a detectable antibody by transfecting cells with vector encoding 5'-3' a single chain antibody, a flexible glycine linker, and GFP (Casey et al., page 446, Figure 1, construct iv). Casey et al. further provides motivation for making a chimeric antibody comprising GFP as a detectable marker by teaching that fluorescent labels provide high levels of sensitivity for a wide range of analytical assays (Casey et al., page 445, column 1 paragraph 2). In addition, the skilled artisan would be motivated to use a fluorescent antibody over an antibody linked to an enzymatic protein based on the fact that fluorescent antibodies can be directly detected without the need to treat the cells or purified antibodies with additional reagents such as X-gal in the case of beta-galactosidase. Therefore, in view of the motivation to make a genetically modified chimeric antibody that is linked to GFP, it would have been *prima facie* obvious at the time of filing for the skilled artisan to substitute GFP for the

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detectable enzymes taught by Fell et al.. Further, based on the successful production of a chimeric GFP-antibody taught by Casey et al, and the high level of skill in the art of molecule biology at the time of filing, the skilled artisan would have had a reasonable expectation of success in modifying the homologous recombination vectors taught by Fell et al. to include a flexible linker attached to GFP.

Claims 1-9 and 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,202,238 (1993), hereafter referred to as Fell et al., in view of Casey et al. (June 2000) Prot. Engineer., Vol. 13(6) 445-452 as applied to claims 20-21, and 27-30 above, and further in view of U.S. Patent No. 6,570,061 (2003), hereafter referred to as Rajewsky et al. The applicant claims genetically modified mammals which express a chimeric immunoglobulin gene comprising a gene expressing an immunoglobulin component linked to a polynucleotide encoding a detectable protein or peptide, wherein the immunoglobulin component includes kappa or lambda light chain components, or heavy chain components. The applicant further claims said mammals wherein the polynucleotide encoding the detectable protein is present at the C-terminus of the gene product with a flexible linked therebetween and located in exon G1. In addition, the applicant claims said mammals wherein the detectable marker is an autofluorescent protein such as green fluorescent protein (GFP).

As discussed in detail above, Fell et al. in view of Casey et al. provide the teaching and motivation to use homologous recombination to replace a heavy or light chain constant region gene with a detectable enzyme or GFP, or all or a portion of a human constant region gene linked to a detectable enzyme or GFP. As noted above, Fell et al. in view of Casey et al. also

provides teaching and motivation for inclusion of a flexible peptide linker between the immunoglobulin component and GFP, and for inclusion of the detectable marker in the G1 exon.

Fell et al. and Casey et al. differ from the claims as written by failing to teach a genetically modified mammal. Both Fell et al. and Casey et al. teach genetically modified cells. Rajewsky et al. supplements the teachings of Fell et al. and provides motivation for making genetically modified mammals instead of genetically modified cells. As noted above, Fell et al. teaches homologous recombination in antibody producing cells to replace a constant region gene with all or a portion of a human constant region gene linked to a detectable enzyme. Rajewsky et al. teaches the use of homologous recombination to replace the constant region genes of the murine immunoglobulin heavy or light chain with human genes in murine embryonic stem cells, and the further use of these cells to make transgenic mice which produce the chimeric antibody (Rajewsky et al., abstract, columns 5-6, and claims 31). Rajewsky et al. further provides motivation for making transgenic mammals to produce chimeric antibodies over *in vitro* methods of producing antibodies using recombinant cells by teaching that drawbacks to *in vitro* methods of producing chimeric antibodies is the cumbersome work required to generate specific monoclonal antibody of appropriate biological function and the difficulty in producing large quantities of these antibodies (Rajewsky et al., column 1). The use of transgenic mice overcomes these obstacles since every cell possesses the inserted replacement gene such that exposure to different antigens will produce chimeric antigen-specific antibodies in quantities substantially larger than the amount capable of being expressed by cells in tissue culture. Based on the benefits to producing chimeric antibodies using transgenic mice over recombinant cells in tissue culture, it would have been *prima facie* obvious to the skilled artisan at the time of filing to use

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the homologous recombination vector taught by Fell et al. to produce transgenic mice according to the methodology taught by Rajewsky et al. Since Fell et al. teaches successful homologous recombination of cells using their disclosed vectors, the skilled artisan would have had a reasonable expectation of success in using these vectors to insert the replacement gene into murine embryonic stem cells instead of antibody producing immune cells.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 872-9306.

**Please note that the United States Patent and Trademark Office will begin to move to the new campus in Alexandria, Virginia, in December 2003. The examiners of Art Unit 1632 will be moving in January 2004. As of January 13, 2004, this examiner's phone number will be (571) 272-0737, and that of the examiner's supervisor will be (571) 272-0734.**

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D  
PRIMARY EXAMINER

